METHOD STATEMENT

Determinand:
Benzotriazole, Ciprofloxacin, 5-Methyl-1H-Benzotriazole, Azithromycin, Carbamazepine, Carbamazepine-10,11-epoxide, Propranolol, Norerythromycin, Erythromycin, Fluoxetine, Clarithromycin, Atorvastatin, 2-Hydroxy-Atorvastatin, 4-Hydroxy-Atorvastatin, Sertraline, Norsertraline, Diclofenac, Ranitidine, Atenolol, PFOA and PFOS

Matrix:
Untreated sewage effluents, treated sewage effluents and surface waters

Principle of Method:
The pharmaceuticals are isolated from aqueous matrix using solid phase extraction (SPE) and eluted from the SPE cartridges with methanol. The extract is blown down to 200ul and transferred to an insert vial to be blown down further to 100ul The extract is quantified by high resolution, accurate mass (HRAM) liquid chromatography mass spectrometry (LC-MS), using a gradient elution run for all determinands except Atenolol and Ranitidine, which are acquired via an isocratic run.

Sampling and Sample Preparation:
Samples should be taken in 250ml glass bottle. No preservative is required.
Samples are stored at 3 ± 2˚C prior to analysis.
Samples are stable for times stated below, from sampling.

1,2,3-Benzotriazole	15 days (in-house data)
Tolyltriazole	15 days (in-house data)
Ciprofloxacin	7 days (in-house data)

Interferences:
The LC-MS system operates at a mass spectral resolution of 70,000 FWHM and therefore the technique is extremely selective, however in theory any substance with an equivalent LC retention time, and which generates ions within a 5ppm window of the analyte's m/z may interfere.

Performance of Method:

Determinand	LOD ng/l	MRL ng/l	Range (MRL -)	Low Std		High Std	
				%RSD	%Bias	%RSD	%Bias
Benzotriazole	1.0341	2	500	11.78	9.61	7.47	4.58
Carbamazepine	0.2772	1	2000	3.98	3.95	3.46	-1.49
Atenolol	0.1930	1	200	8.28	1.05	6.58	-1.42
Fluoxetine	0.0469	0.2	200	5.27	-0.28	3.52	-0.70
Propranolol HCl	0.0458	0.2	200	4.39	0.84	3.06	-1.78
Erythromycin	2.3053	10	2000	3.69	1.84	3.00	-3.29
Azithromycin	0.0520	0.2	100	12.22	-2.96	7.54	-3.27
Ciprofloxacin	0.7487	2	200	8.85	-3.92	7.09	-4.40
Ranitidine HCl	0.9814	5	2000	10.41	-5.99	12.23	-1.47
Atorvastatin Calcium Salt	0.2733	1	200	7.47	-5.42	6.04	-4.89
Norerythromycin HCl	0.5541	2	2000	6.75	2.94	5.57	-5.01
Sertraline HCl	0.0510	0.2	200	5.00	-1.06	2.75	-1.41
2-Hydroxy Atorvastatin	0.3586	2	200	7.75	-5.13	5.40	-3.21
4-Hydroxy Atorvastatin	1.5087	2	200	9.75	1.42	12.80	-2.15

METHOD STATEMENT

Determinand	LOD ng/l	MRL ng/l	Range (MRL -)	Low Std		High Std	
				%RSD	%Bias	%RSD	%Bias
Carbamazepine-10,11-epoxide	0.0477	0.2	2000	5.27	4.07	3.77	-2.60
Norsertraline HCl	0.4890	2	200	5.87	-5.42	7.31	-0.05
Diclofenac	0.9629	2	200	4.08	-0.91	3.22	-0.03
5-Methyl-1H-Benzotriazole	0.8183	2	500	12.66	0.26	9.73	5.02
Clarithromycin	0.2510	1	200	9.45	0.85	9.37	-3.58
PFOA	0.1160	0.65	20	-	-	0.45	-0.23
PFOS	0.1172	0.65	20	-	-	1.34	-0.24

Determinand	Spike (ng/L)	Finham Final Effluent		Bulkington Crude	
		%RSD	%Rec.	%RSD	%Rec.
Benzotriazole	8	16.38	90.70	-	-
	32	10.18	100.47	9.31	100.08
Carbamazepine	400	12.64	91.47	-	-
	1600	12.20	92.68	3.51	102.02
Atenolol	40	7.92	101.79	-	-
	160	5.80	100.78	6.29	99.55
Fluoxetine	40	6.13	99.42	-	-
	160	3.54	99.70	3.63	99.12
Propranolol	40	6.58	101.47	-	-
	160	3.28	98.75	3.10	98.19
Erythromycin	400	4.43	105.41	-	-
	1600	2.54	98.23	2.45	97.39
Azithromycin	20	13.22	98.15	-	-
	80	10.67	103.09	8.19	99.68
Ciprofloxacin	40	14.45	89.77	-	-
	160	6.81	91.76	9.77	90.42
Ranitidine	400	18.74	104.75	-	-
	1600	20.10	93.17	18.94	91.02
Atorvastatin	40	9.42	95.78	-	-
	160	4.44	95.16	6.80	93.75
Norerythromycin	400	9.30	89.97	-	-
	1600	6.70	86.91	8.78	98.17
Sertraline	40	6.53	98.64	-	-
	160	2.81	100.57	2.72	99.23
2-Hydroxyatorvastatin	40	8.88	95.00	-	-
	160	4.72	96.60	5.10	96.30
4-Hydroxyatorvastatin	40	11.47	101.18	-	-
	160	7.27	100.66	9.32	97.43
Carbamazepine-10,11-epoxide	400	5.39	105.59	-	-
	1600	2.77	98.92	4.13	112.00
Norsertraline	40	6.68	92.28	-	-
	160	6.03	99.73	6.01	98.55
Diclofenac	40	6.09	100.34	-	-
	160	3.04	100.81	2.92	100.62
5-Methyl-1H-Benzotriazole	8	13.15	92.97		
	32	11.97	102.35	11.39	101.21
Clarithromycin	40	9.21	99.70	-	-
	160	10.57	98.10	9.77	95.84

METHOD STATEMENT

Determinand	Spike (ng/L)	Finham Final Effluent		Bulkington Crude	
		%RSD	%Rec.	%RSD	%Rec.
PFOA	4	-	-	-	-
	16	1.40	98.41	-	-
PFOS	4	-	-	-	-
	16	1.42	100.73	-	-

Uncertainty of Measurement:

The Uncertainty of Measurement has been calculated following the guidelines provided by the CIP2 Technical Specification.

Determinand	Uncertainty of Measurement %
All Compounds	50

References:
In-house method – no external references